

Claims

- 5 1. A method of identifying a condition in an individual in which an elevated serum or plasma HDL concentration, or HDL cholesterol concentration, provides enhanced protection against cardiovascular disease, the method comprising the step of testing the individual for a disorder that detrimentally affects the protective effect of HDL, whereby absence of such a disorder is an indication of enhanced protection against cardiovascular disease when said individual exhibits elevated serum or plasma HDL or HDL cholesterol concentration.
- 10 2. The method according to claim 1, wherein the disorder is selected from liver damage and oxidative stress.
- 15 3. The method according to claim 1 or 2, comprising the additional step of determining the serum or plasma HDL or HDL cholesterol concentration.
- 20 4. The method according to claim 2 wherein the disorder comprises liver damage and testing for liver damage comprises determining γ -glutamyltransferase or a liver transaminase activity or concentration in a serum or plasma sample and comparing it to a selected reference value for γ -glutamyltransferase.
- 25 5. The method according to claim 2, wherein the disorder comprises liver damage and testing for liver damage comprises genotyping mutations or polymorphisms inducing or predisposing to liver damage or influencing serum or plasma γ -glutamyltransferase activity or concentration or the testing of the expression of the genes encoding these proteins.
- 30 6. The method according to claim 2, wherein the disorder comprises oxidative stress and testing for oxidative stress comprises determining serum or plasma ac-

tivity or concentration of one or several phase I or phase II detoxification enzyme.

- 5 7. The method according to claim 2, wherein the disorder comprises oxidative
stress and testing of oxidative stress is the assessment of serum or plasma con-
centration of ferritin or an oxidized fatty acid, oxidized phospholipid or choles-
terol oxidation product.
- 10 8. The method according to claim 6, wherein the detoxification enzyme is a cyto-
chrome P450 enzyme or the catalase, a paraoxonase, a superoxide dismutase, a
glutathione peroxidase, a glutathione synthase, a glutathione reductase, a glu-
tathione transferase, a glutamyl-cysteinyl synthase, a quinone reductase, a
diaphorase, a thioredoxin, a glutaredoxin, a peroxiredoxin, an epoxide hydrolase,
an aldehyde hydrolase, an aldo-keto reductase, a properdin, the selenoproteins P
or W, an N-acetyl-transferase, a metallothionein, a sulfurtransferase, an alcohol
dehydrogenase, an aldehyde dehydrogenase, a glutamate dehydrogenase, a dihy-
drodiol dehydrogenase, or a carboxyl esterase.
- 15 9. The method according to claim 2, wherein the disorder comprises oxidative
stress and testing for oxidative stress comprises determining the antioxidantive
capacity of HDL
- 20 10. The method according to claim 4, wherein the reference value is selected from a
reference range of 20 to 100 units per liter.
- 25 11. The method according to any one of the preceding claims, wherein the cardio-
vascular disease is coronary heart disease or cerebrovascular disease.
- 30 12. The method according to claim 11, wherein the coronary heart disease is myo-
cardial infarction.

- 5 13. Method of treatment of an individual in order to protect the said individual against the risk of cardiovascular disease, the method comprising the steps of testing the said individual for a disorder which detrimentally affects the protective effect of HDL, identifying and selecting an individual free of said condition, and treating the selected individual in order to enhance the HDL or HDL cholesterol level of said individual.
- 10 14. The method according to claim 13, wherein the disorder is selected from liver damage and oxidative stress.
- 15 15. The method according to claim 14, wherein the disorder comprises liver damage and testing for liver damage comprises determining γ -glutamyltransferase activity or concentration in a serum or plasma sample and comparing it to a selected reference value for γ -glutamyltransferase.
- 20 16. The method according to claim 14, wherein the disorder comprises liver damage and testing for liver damage comprises genotyping mutations or polymorphisms influencing serum or plasma γ -glutamyltransferase activity or concentration, or mutations in the phase I and II enzymes, or the expression of these genes.
- 25 17. The method according to claim 14, wherein the disorder comprises oxidative stress and testing for oxidative stress comprises determining serum or plasma paraoxonase activity or concentration.
- 30 18. The method according to claim 14, wherein the disorder comprises oxidative stress and testing for oxidative stress comprises determining the antioxidant capacity of HDL
19. The method according to claim 13, wherein the treatment to enhance the HDL or HDL cholesterol level is a drug treatment, the drug being selected from the group consisting of niacin, a statin, an apolipoprotein AI or AII synthesis en-

hancing agent, a PPAR alpha agonist such as a fibrate, a PPAR gamma or delta agonist, a sterol absorption inhibiting agent such as a resin, a CETP inhibitor, an ACAT inhibitor, a PLTP agonist, a LCAT agonist, a LPL agonist, a hepatic li-
pase agonist, a SR-B1 agonist, or a ABC1 (ATP-binding cassette A1) agonist.

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20. The method according to claim 19, wherein the statin is selected from the group consisting of atorvastatin, fluvastatin, lovastatin, pravastatin and simvastatin.

10 21. The method according to claim 19, wherein the fibrate is selected from the group consisting of bezafibrate, ciprofibrate, clofibrate, fenofibrate and gemfibrozil.

22. The method according to claim 19, wherein the resin is selected from the group consisting of colestipol and cholestyramin.

15 23. The method according to claim 13, wherein the treatment includes physical ac-
tivity or physical exercise.

24. The method according to claim 13, wherein the treatment includes gene transfer
and other kinds of gene therapy.

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25. A kit for identifying a condition in an individual in which condition an elevated serum or plasma HDL or HDL cholesterol concentration provides enhanced pro-
tection against cardiovascular disease, or for predicting an individual's response to HDL or HDL cholesterol elevating treatments, wherein the kit comprises
means for testing the individual for a disorder which detrimentally affects the protective effect of HDL

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26. The kit according to claim 25, wherein the additional condition is liver damage
and the means comprise means for determining serum or plasma γ -
glutamyltransferase or for genotyping genomic mutations and/or polymorphisms.

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27. The kit according to claim 25, wherein the additional condition is oxidative stress and the means comprise means for determining paraoxonase activity or concentration, the antioxidative capacity of HDL, or genotyping genomic mutations and polymorphisms.

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28. The kit according to claim 25 for assessing an individual's risk of cardiovascular disease further comprising means for determining HDL or HDL cholesterol concentration in a serum or plasma sample of said individual.

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